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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,555	02/25/2002	Michael G. Goggins	JHU1700-1	7972

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,555	GOGGINS ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a) In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U S C § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment See 37 CFR 1 704(b)

Status

1)☒ Responsive to communication(s) filed on *07 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,10-15,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10-15,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2/3/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's preliminary amendment filed on August 7, 2003 is acknowledged. Claims 1-6, 9 and 16-21 have been canceled. Claim 7 has been amended. Claims 22 and 23 have been added. Claims 7-8, 10-15 and 22-23 are pending.

2. Applicant's election with traverse of Group II, claims 7-15, and the human preproenkaphalin A gene filed on August 7, 2003 is acknowledged. However, the arguments are deemed moot in view of Applicant's preliminary amendment. Additionally, the restriction requirement for the specific primer pair have been withdrawn in view of Applicant's preliminary amendment. Accordingly, the gene preproenkaphalin A gene and SEQ ID NOS: 115-118 along with claims 7-8, 10-15, 22 and 23 have been searched.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Objections

4. The disclosure and claim 22 are objected to because of the following informalities:

(a) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at paragraph 0037. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code by removing the "www". See MPEP § 608.01.

(b) In claim 22, the word "methd" is misspelled. It is suggested changing "methd" to --method--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 7-8, 10-15 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting a cellular proliferative disorder associated with pancreatic cancer or colorectal cancer, it does not reasonably provide enablement for a method for detecting any of the plethora of cellular proliferative disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The first paragraph of section 112 requires the specification describe how to make or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factor include, but are not limited to:

I. Quantity of Experimentation Necessary

The claimed invention is drawn to "a method for detecting a cellular proliferative disorder in a subject comprising: a) contacting a nucleic acid-containing specimen from the subject with an agent that provides a determination of the methylation state of Preproenkephalin A (ppENK) gene; and (b) identifying aberrant methylation of regions of the gene or regulatory region, wherein aberrant methylation is identified as being different when compared to the same regions of the gene or associated regulatory region in a subject not having said cellular

proliferative, thereby detecting a cellular proliferative disorder in the subject". At page 6, the specification teaches that the present invention is paged on the finding that several genes are newly identified as being differentially methylated in cancer. At pages 7 and 8, the specification summarizes the embodiments of the invention and state at paragraph 0019 that in a preferred embodiment, the cell proliferative disorder is pancreatic carcinoma. The figures and detailed description of the invention teach wherein pancreatic cancer cells versus normal pancreata were analyzed to determine methylation state. At page 14, the specification discloses wherein normal gastric, duodenal and colonic musosae were analyzed to determine methylation state and further at page 21, discuss wherein genes differentially methylated in colorectal cancer were identified. Likewise the examples at pages 38-48 only discuss wherein the claimed method was performed on pancreatic adenocarcinoma cell lines versus normal pancreata. Despite statements in the specification that the method is applicable to numerous cellular proliferative disorders such as e.g., low grade astrocytoma, anaplastic astrocytoma, glioblastoma, medulloblastoma, gastric cancer, colorectal adenoma, acute myelogenous leukemia, lung cancer, renal cancer, leukemia, breast cancer, prostate cancer, endometrial cancer and neuroblastoma, colon cancer, lung cancer, breast cancer, prostate cancer, and melanoma, there is no enabling disclosure relating said method to any of the many other disorders recited above. Likewise, there is no indication from the specification that the methylation state of the gene ppENK is affected in any cellular proliferative disorder or those recited above, other than pancreatic cancer and colorectal cancer. More specifically, the specification does not provide any information to enable one of ordinary skill in the art to use the claimed invention to detect any cellular proliferative disorder by determining the methylation state of ppENK gene. As to quantity of experimentation required,

one of skill in the art would have to design an experimental protocol which would provide analysis of other cellular proliferative disorders. In other words, considerable new research would be required.

II. Amount of Direction and Guidance

The specification does not provide any reasonable method for detecting a cellular proliferative disorder that bears a reasonable correlation to the entire scope of the claims. The examples beginning at page 38 lack information concerning how to use the invention for detecting other cellular proliferative disorders, besides pancreatic cancer. The specification does not provide any guidance as to how determination of the methylation state of the gene, ppENK, is associated with or is relevant to the detection of any cellular proliferative disorder, other than pancreatic cancer. In order to utilized the invention commensurate fully in scope, would require undue experimentation to the practitioner.

III. Presence and Absence of Working examples

The specification of the claimed invention lacks proper working examples. At page 38, the specification teaches collection and preparation of pancreatic cell lines. At page 39, the specification teaches methylated CpG island amplification and representational difference analysis in carcinoma of the pancreas versus normal pancreata. At page 40, the specification teaches DNA sequencing and dot blot hybridization procedures performed in pancreatic cancer cells and normal pancreas. At pages 41-48, the examples 4-13, all discloses wherein cells or specimens were obtained from pancreatic adenocarcinomas versus normal tissue. Nowhere in the example does the specification teach wherein the claimed method was performed on cells related to other cellular proliferative disorders, besides pancreatic cancer. Nowhere in the

examples does the specification disclose, relate or correlate the methylation state of the gene ppENK to the detection of any cellular proliferative disorder, besides pancreatic cancer. Likewise, nowhere in the examples is there a teaching wherein the methylation state of any gene is associated with the detection of a cellular proliferative disorder. Merely making reference to the method being applicable to numerous cellular proliferative disorder and specimen-types does not enable the practitioner to reproduce the results as claimed for the broad scope of the claimed invention.

IV. The Nature of the Invention

The nature of the inventions is "a method for detecting a cellular proliferative disorder in a subject comprising: a) contacting a nucleic acid-containing specimen from the subject with an agent that provides a determination of the methylation state of Preproenkephalin A (ppENK) gene; and (b) identifying aberrant methylation of regions of the gene or regulatory region, wherein aberrant methylation is identified as being different when compared to the same regions of the gene or associated regulatory region in a subject not having said cellular proliferative, thereby detecting a cellular proliferative disorder in the subject". The full scope of the claimed invention is not reproducible due to the lack of guidance provided in the specification. As noted, the specification does properly disclose a method of detecting a cellular proliferative disorder that bears a reasonable correlation to the entire scope of the claims.

V. Level of Predictability and Unpredictability in the Art

The specification has not enabled a method of detecting a cellular proliferative disorder by determining the methylation state of ppENK gene that is commensurate fully in scope. The level of skill in the art at the time of the invention is very high, however the level of

unpredictability in molecular biology is also high. Although certain techniques useful in the claimed invention were known in the art, the art does not teach a method of detecting a cellular proliferative disorder by determining the methylation state of ppENK gene as described in the claimed invention.

For all of the forgoing reasons, undue experimentation is necessary for one of skill in the art to obtain the claimed invention.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 7,8, 10-15, 22, 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 7, 8, 10-15, 22, and 23 are indefinite in claim 7 for "ppENK" because abbreviations often have more than one meaning in the art. It is suggested inserting the full name of the abbreviation as supported by the specification into the claim.

Conclusion

6. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308 0196.

CYNTHIA WILDER
PATENT EXAMINER

Cynthia B. Wilder, Ph.D.
Examiner
Art Unit 1637

November 12, 2003